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(54) Title: NOVEL GENES ENCODING PROTEINS HAVING PROGNOSTIC, DIAGNOSTIC, PREVENTIVE, THERAPEUTIC, AND OTHER USES

(57) Abstract: The invention provides isolated nucleic acids encoding a variety of proteins having diagnostic, preventive, therapeutic, and other uses. These nucleic and proteins are useful for diagnosis, prevention, and therapy of a number of human and other animal disorders. The invention also provides antisense nucleic acid molecules, expression vectors containing the nucleic acid molecules of the invention, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a nucleic acid molecule of the invention has been introduced or disrupted. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides and antibodies. Diagnostic, screening, and therapeutic methods utilizing compositions of the invention are also provided. The nucleic acids and polypeptides of the present invention are useful as modulating agents in regulating a variety of cellular processes.

What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule having a nucleotide sequence which is at least 40% identical to the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

b) a nucleic acid molecule comprising at least 15 nucleotide residues and having a nucleotide sequence identical to at least 15 consecutive nucleotide residues of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

c) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

d) a nucleic acid molecule which encodes a polypeptide having an amino acid sequence comprising at least 8 consecutive amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438; and

e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, wherein the nucleic acid molecule hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

a) a nucleic acid having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof; and

b) a nucleic acid molecule which encodes a polypeptide having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

3. The nucleic acid molecule of claim 1, further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous polypeptide.

5. A host cell which contains the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

a) a fragment of a polypeptide having an amino acid sequence comprising at least 8 contiguous amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-

76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438;

b) a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions; and

c) a polypeptide which is encoded by a nucleic acid molecule having a nucleotide sequence which is at least 40% identical to any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

9. The isolated polypeptide of claim 8, having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

10. The polypeptide of claim 8, wherein the amino acid sequence of the polypeptide further comprises heterologous amino acid residues.

11. An antibody which selectively binds with the polypeptide of claim 8.

12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

b) a polypeptide having an amino acid sequence which comprises at least 8 contiguous amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438; and

c) a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions;

the method comprising culturing the host cell of claim 5 under conditions in which the nucleic acid molecule is expressed.

13. A method for detecting the presence of a polypeptide of claim 8 in a sample, comprising:

a) contacting the sample with a compound which selectively binds with a polypeptide of claim 8; and

b) determining whether the compound binds with the polypeptide in the sample.

14. The method of claim 13, wherein the compound which binds with the polypeptide is an antibody.

15. A kit comprising a compound which selectively binds with a polypeptide of claim 8 and instructions for use.

16. A method for detecting the presence of a nucleic acid molecule of claim 1 in a sample, comprising the steps of:

a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes with the nucleic acid molecule; and

b) determining whether the nucleic acid probe or primer binds with a nucleic acid molecule in the sample.

17. The method of claim 16, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

18. A kit comprising a compound which selectively hybridizes with a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which binds with a polypeptide of claim 8 comprising the steps of:

a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and

b) determining whether the polypeptide binds with the test compound.

20. The method of claim 19, wherein the binding of the test compound with the polypeptide is detected by a method selected from the group consisting of:

a) detection of binding by direct detecting of test compound/polypeptide binding;

b) detection of binding using a competition binding assay;

c) detection of binding using an assay for an activity characteristic of the polypeptide.

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds with the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.

22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

a) contacting a polypeptide of claim 8 with a test compound; and

b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

23. An antibody substance which selectively binds with the polypeptide of claim 8, wherein the antibody substance is made by providing the polypeptide to an immunocompetent vertebrate and thereafter harvesting blood or serum from the vertebrate.

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                                                                M   K   R   L   L   L   L   F        8
CGGACGCGGTGGGCGGACGCGTGGGCAGCTGAAGAAAGAGAGGA ATG AAG CGC CTT CTG CTT CTG TTT        68

 L   F   F   I   T   F   S   S   A   F   P   L   V   R   M   T   E   N   E   E    28
TTG TTC TTT ATA ACA TTT TCT TCT GCA TTT CCC TTA GTC CGG ATG ACG GAA AAT GAA GAA   128

 N   M   Q   L   A   Q   A   Y   L   N   Q   F   Y   S   L   E   I   E   G   N    48
AAT ATG CAA CTG GCT CAG GCA TAT CTC AAC CAG TTC TAC TCT CTT GAA ATA GAA GGG AAT   188

 H   L   V   Q   S   K   N   R   S   L   I   D   D   K   I   R   E   M   Q   A    68
CAT CTT GTT CAA AGC AAG AAT AGG AGT CTC ATA GAT GAC AAA ATT CGG GAA ATG CAA GCA   248

 F   F   G   L   T   V   T   G   K   L   D   S   N   T   L   E   I   M   K   T    88
TTT TTT GGA TTG ACA GTG ACT GGA AAA CTG GAC TCA AAC ACC CTT GAG ATC ATG AAG ACA   308

 P   R   C   G   V   P   D   V   G   Q   Y   G   Y   T   L   P   G   W   R   K   108
CCC AGG TGT GGG GTG CCT GAT GTG GGC CAG TAT GGC TAC ACC CTC CCT GGG TGG AGA AAA   368

 Y   N   L   T   Y   R   I   I   N   Y   T   P   D   M   A   R   A   A   V   D   128
TAC AAC CTC ACC TAC AGA ATA ATA AAC TAT ACT CCG GAT ATG GCA CGA GCT GCT GTG GAT   428

 E   A   I   Q   E   G   L   E   V   W   S   K   V   T   P   L   K   F   T   K   148
GAG GCT ATC CAA GAA GGT TTA GAA GTG TGG AGC AAA GTC ACT CCA CTA AAA TTC ACC AAG   488
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Fig. 1A

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 I   S   K   G   I   A   D   I   M   I   A   F   R   T   R   V   H   G   R   C   168
ATT TCA AAG GGG ATT GCA GAC ATC ATG ATT GCC TTT AGG ACT CGA GTC CAT GGT CGG TGT   548

 P   R   Y   F   D   G   P   L   G   V   L   G   H   A   F   P   P   G   P   G   188
CCT CGC TAT TTT GAT GGT CCC TTG GGA GTG CTT GGC CAT GCC TTT CCT CCT GGT CCG GGT   608

 L   G   G   D   T   H   F   D   E   D   E   N   W   T   K   D   G   A   G   F   208
CTG GGT GGT GAC ACT CAT TTT GAT GAG GAT GAA AAC TGG ACC AAG GAT GGA GCA GGA TTC   668

 N   L   F   L   V   A   A   H   E   F   G   H   A   L   G   L   S   H   S   N   228
AAC TTG TTT CTT GTG GCT GCT CAT GAA TTT GGT CAT GCA CTG GGG CTC TCT CAC TCC AAT   728

 D   Q   T   A   L   M   F   P   N   Y   V   S   L   D   P   R   K   Y   P   L   248
GAT CAA ACA GCC TTG ATG TTC CCA AAT TAT GTC TCC CTG GAT CCC AGA AAA TAC CCA CTT   788

 S   Q   D   D   I   N   G   I   Q   S   I   Y   G   G   L   P   K   V   P   A   268
TCT CAG GAT GAT ATC AAT GGA ATC CAG TCC ATC TAT GGA GGT CTG CCT AAG GTA CCT GCT   848

 K   P   K   E   P   T   I   P   H   A   C   D   P   D   L   T   F   D   A   I   288
AAG CCA AAG GAA CCC ACT ATA CCC CAT GCC TGT GAC CCT GAC TTG ACT TTT GAC GCT ATC   908

 T   T   F   R   R   E   V   M   F   F   K   G   R   H   L   W   R   I   Y   Y   308
ACA ACT TTC CGC AGA GAA GTA ATG TTC TTT AAA GGC AGG CAC CTA TGG AGG ATC TAT TAT   968
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Fig. 1B

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 D   I   T   D   V   E   F   E   L   I   A   S   F   W   P   S   L   P   A   D  328
GAT ATC ACG GAT GTT GAG TTT GAA TTA ATT GCT TCA TTC TGG CCA TCT CTG CCA GCT GAT 1028

 L   Q   A   A   Y   E   N   P   R   D   K   I   L   V   F   K   D   E   N   F  348
CTG CAA GCT GCA TAC GAG AAC CCC AGA GAT AAG ATT CTG GTT TTT AAA GAT GAA AAC TTC 1088

 W   M   I   R   G   Y   A   V   L   P   D   Y   P   K   S   I   H   T   L   G  368
TGG ATG ATC AGA GGA TAT GCT GTC TTG CCA GAT TAT CCC AAA TCC ATC CAT ACA TTA GGT 1148

 F   P   G   R   V   K   K   I   D   A   A   V   C   D   K   T   T   R   K   T  388
TTT CCA GGA CGT GTG AAG AAA ATA GAT GCA GCC GTC TGT GAT AAG ACC ACA AGA AAA ACC 1208

 Y   F   F   V   G   I   W   C   W   R   F   D   E   M   T   Q   T   M   D   K  408
TAC TTC TTT GTG GGC ATT TGG TGC TGG AGG TTT GAT GAA ATG ACC CAA ACC ATG GAC AAA 1268

 G   F   P   Q   R   V   V   K   H   F   P   G   I   S   I   R   V   D   A   A  428
GGA TTC CCG CAG AGA GTG GTA AAA CAC TTT CCT GGA ATC AGT ATC CGT GTT GAT GCT GCT 1328

 F   Q   Y   K   G   F   F   F   F   S   R   G   S   K   Q   F   E   Y   N   I  448
TTC CAG TAC AAA GGA TTC TTC TTT TTC AGC CGT GGA TCA AAG CAA TTT GAA TAC AAC ATT 1388

 K   T   K   N   I   T   R   I   M   R   T   N   T   W   F   Q   C   K   E   P  468
AAG ACA AAG AAT ATT ACC CGA ATC ATG AGA ACT AAT ACT TGG TTT CAA TGC AAA GAA CCA 1448
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Fig. 1C

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 K   N   S   S   F   G   F   D   I   N   K   E   K   A   H   S   G   G   I   K   488
AAG AAC TCC TCA TTT GGT TTT GAT ATC AAC AAG GAA AAA GCA CAT TCA GGA GGC ATA AAG 1508

 I   L   Y   H   K   S   L   S   L   F   I   F   G   I   V   H   L   L   K   N   508
ATA TTG TAT CAT AAG AGT TTA AGC TTG TTT ATT TTT GGT ATT GTT CAT TTG CTG AAA AAC 1568

 T   S   I   Y   Q   *                                                         514
ACT TCT ATT TAT CAA TAA                                                       1586

ATTCATAGACCTAAAATAAACCTCAACAGGTCTTTTAATATAAATTCTGCTTCAAAATAGAATAAAACCATTCTTTAAC 1665

AACAAAAAAAAAAAAAAA                                                            1684
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Fig. 1D